Biohaven Advances Development of the MoDE Platform Technology Licensed From Yale University

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- *Biohaven advances development of its extracellular target degrader platform technology (MoDEs™) for therapies across a variety of diseases including neuroscience, immunology and oncology*
- *Through its continued collaboration with Yale University in the laboratory of Professor David Spiegel and Biohaven Labs, Biohaven has made further innovations in this ground-breaking technology with new patent applications covering additional targets and functionality*
- *In-licensed from Yale University in 2021, the MoDE platform is based on patent applications filed by Yale in 2018 and 2019*

NEW HAVEN, Conn., Oct. 25, 2022 /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN; "Biohaven") today announced advancements in the development of its MoDE extracellular target degrader platform technology licensed from Yale University for various disease indications, including, but not limited to, neurological disorders, cancer, infectious and autoimmune diseases.

In 2021, Biohaven entered into a worldwide, exclusive license agreement to develop and commercialize the MoDE platform based on ground-breaking research conducted in the laboratory of Professor David Spiegel at Yale University. Under the license agreement, Biohaven acquired exclusive, worldwide rights to Yale's intellectual property directed to its MoDE technology, which pertains to the clearance of disease-causing proteins and other biomolecules by targeting them for lysosomal degradation using multi-functional molecules.

Professor Spiegel commented: "Targeted protein degradation (TPD) has emerged as a promising and exciting therapeutic strategy, however, the majority of existing TPD technologies to date rely on the ubiquitin-proteasome system that targets intracellular proteins. To address this limitation, our lab developed MoDEs, a class of modularly designed, bifunctional synthetic molecules, which are capable of mediating the degradation of extracellular proteins through the asialoglycoprotein receptor (ASGPR). MoDE molecules mediate the formation of a ternary complex between a target protein and the ASGPR, which is expressed primarily on hepatocytes, and the target protein is then endocytosed and degraded by lysosomal proteases. The MoDE platform is differentiated from existing approaches, such as Proteolysis Targeting Chimeras (PROTAC), in that it does not rely on ubiquitin ligases, and allows for a broad range of targets to be degraded."

Through the novel approach, Professor Spiegel demonstrated the modularity of the MoDE technology by synthesizing bifunctional molecules that induce the degradation of both antibody and pro-inflammatory cytokine proteins. When initially published, the data obtained by the Spiegel Lab represented the first experimental evidence that non-proteinogenic, synthetic molecules could be employed for the TPD of extracellular proteins both *in vitro* and *in vivo*.

The MoDE platform discovered at Yale University is described in a peer-reviewed publication entitled "Bifunctional Small Molecules that Mediate the Degradation of Extracellular Proteins" (*Nature Chemical Biology* 2021, 17, 947–953) and in various Yale University patent applications, including applications published as WO 2019/199621 and WO 2019/199634, both of whom are based on provisional applications filed in 2018. Subsequent to the Yale patent filings, others have referred to such multifunctional molecules for extracellular protein degradation as "ASGPR Targeting Chimeras" (ATACs) (see, for example, https://endpts.com/an-ra-backed-startup-atacs-a-novel-challenge-looking-to-spur-protein-degradation-outside-the-cell) or "Lysosome-Targeting Chimeras" (LyTACs) (see, for example, https://endpts.com/going-where-protacs-cant-versant-unveils-50m-bet-on-carolyn-bertozzis-lytac-tech-with-a-seasoned-biotech-exec-at-the-helm). Both Yale and Biohaven continue to expand the intellectual property portfolio underlying the platform with a series of new applications filed worldwide that disclose and claim various aspects of the multifunctional degraders and methods for their use. Since entering into the license agreement with Yale in 2021, Yale has filed more than eight additional patent applications covering this technology.

About Biohaven.
Biohaven is a global clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of life-changing therapies for people with debilitating neurological and neuropsychiatric diseases, including rare disorders. Biohaven is advancing a pipeline of best-in-class therapies for diseases with little or no treatment options, leveraging its proven drug development capabilities and proprietary platforms, including Kv7 ion channel modulation for epilepsy and neuronal hyperexcitability; glutamate modulation for obsessive-compulsive disorder and spinocerebellar ataxia and myostatin inhibition for neuromuscular diseases. Biohaven's portfolio of early- and late-stage product candidates also includes discovery research programs focused on TRPM3 channel activation for neuropathic pain and CD-38 antibody recruiting, bispecific molecules for multiple myeloma. More information about Biohaven is available at www.biohaven.com.

Forward-Looking Statements
This news release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The use of certain words, including "continue", "plan", "will", "believe", "may", "expect", "anticipate" and similar expressions, is intended to identify forward-looking

statements. Investors are cautioned that any forward-looking statements, including statements regarding the future development, timing and potential marketing approval and commercialization of development candidates are not guarantees of future performance or results and involve substantial risks and uncertainties. Actual results, developments and events may differ materially from those in the forward-looking statements as a result of various factors including: Biohaven's ability to complete the offering of its common shares on the proposed terms, or at all; Biohaven's expectations related to the use of proceeds from the offering of its common shares; the expected timing, commencement and outcomes of Biohaven's planned and ongoing clinical trials; the timing of planned interactions and filings with the FDA; the timing and outcome of expected regulatory filings; complying with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates; the potential for Biohaven's product candidates to be first in class or best in class therapies; and the effectiveness and safety of Biohaven's product candidates. Additional important factors to be considered in connection with forward- looking statements are described in Biohaven's filings with the Securities and Exchange Commission, including within the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The forward-looking statements are made as of the date of this new release, and Biohaven does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

MoDEs is a trademark of Biohaven Therapeutics Ltd.

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